



Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Review

The association between psoriasis and diabetes mellitus: A systematic review and meta-analysis

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ARTICLE INFO

Article history:

Received 5 December 2018

Accepted 14 January 2019

Keywords:

Diabetes mellitus

Psoriasis

Meta-analysis

ABSTRACT

Background: Psoriasis is an immune-mediated chronic inflammatory skin disease with unknown etiology. Current findings demonstrate that psoriatic patients are at higher risk of other systemic disorders such as diabetes mellitus. The present study was conducted to evaluate the association between psoriasis and diabetes mellitus.

Method: The current study was conducted based on preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines. Using MeSH keywords we searched online databases of PubMed, Scopus, Web of Science, Science Direct, Embase, CINAHL, Cochrane Library, EBSCO and Google scholar search engine and the reference list of the retrieved articles until June 2018. Heterogeneity among studies was assessed using Cochran's Q test and I² index and the random effects model was used to estimate Odds Ratio (OR) and 95% confidence interval (CI). Data were analyzed using Comprehensive Meta-Analysis (CMA) software version 2.

Results: Analysis of 38 eligible studies involving 922870 cases and 12808071 controls suggested the estimated OR to be 1.69 (95% Confidence Interval [CI]: 1.51–1.89; P < 0.001). Subgroup analysis was conducted based on study design and country of study and was significant (test for subgroup differences: P = 0.025 and P < 0.001, respectively).

Conclusions: Our study indicated the significant association between psoriasis and diabetes. Therefore, psoriasis is a systemic disorder and other comorbidities should be considered in the management of patients with psoriasis.

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1. Introduction

Psoriasis is an immune-mediated chronic inflammatory skin disease with an estimated prevalence of 2–3% [1]. The etiology of psoriasis is unknown but genetic background, environmental factors and immune system are associated with the risk of psoriasis [2,3]. Interactions between hyperproliferative keratinocytes and immune systems causes psoriasis plaques [4]. Without appropriate treatments, this disease may affect the quality of life [5]. Studies demonstrated that psoriatic patients are at increased risk of other disorders such as Crohn's disease, cardiovascular disease, hypertension, diabetes mellitus and metabolic syndrome, indicating that psoriasis is not limited to skin [6–8]. Diabetes mellitus is a group of

metabolic disorders characterized by hyperglycemia and insufficiency in the production or actions of insulin.

The association between psoriasis and its comorbidities have been assessed by several studies but the results are contradictory. In meta-analyses studies, a full picture of a problem in a certain population can be reported by reviewing all relevant documentation and providing a general evaluation [9,10]. Certainly, with the increase in the number of studies entered in the analysis process, the confidence interval (CI) is decreased and the pooled estimate is more strong [10,11]. Several studies assessed the association between psoriasis and diabetes but there is no concordance between these findings, so the present study was conducted to summarize the results of various studies in a single report.

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2. Method

2.1. Study protocol

We reported a systematic review and meta-analysis based on PRISMA guidelines [12] to assess the association between psoriasis and diabetes based on articles published until June 2018. Two researchers performed all procedures of the study independently and any disagreement between researchers was resolved by a third researcher.

2.2. Search strategy

Search was conducted using MeSH keywords of psoriasis, diabetes and association until June 15, 2018. We searched databases of PubMed, Scopus, Web of Science, Science Direct, Embase, CINAHL, Cochrane Library, EBSCO, and Google scholar search engine and the reference list of the retrieved articles until June 2018 [12]. Mesh keywords included: "Psoriasis" [MeSH], "Diabetes" [MeSH] and "Autoimmune Diseases"[Mesh].

2.3. Inclusion and exclusion criteria

The inclusion criteria were studies addressing the association between psoriasis and diabetes published in English language and the exclusion criteria were: Psoriasis or diabetes not considered as outcome, unpublished studies, review articles, conference presentations, letters to editor and studies without control group.

2.4. Quality assessment

The selected articles were reviewed using the modified Newcastle Ottawa Scale (NOS) for cross sectional and case-control studies. This checklist includes 8 different parts in 4 categories. The lowest acceptable score was considered 7 and the studies that reached this score were included in the study [13].

2.5. Data extraction

In the next step the following data were extracted for each study: author(s) name, country of study, study design, score of quality, name of journal, samples characteristics for patients and controls (e.g. mean age and SD), odds ratio, confidence interval (CI), number of diabetes positive in cases and controls groups.

2.6. Statistical analysis

For assessing the association between psoriasis and diabetes mellitus, we used OR and 95%CI. Evaluation of the heterogeneity among studies was conducted using Cochran's Q test and I^2 Index (The I^2 indexes of lower than 25%, 25–75%, higher than 75% were considered as low, moderate and high heterogeneity, respectively) [14]. The random effects model was used for combining the results of different studies. Sensitivity analysis was conducted by removing one study at a time. To evaluate the causes of heterogeneity, subgroup analysis was performed based on country and study design. Data were analyzed using Comprehensive Meta-Analysis (CMA) software version 2. Publication bias was assessed using Egger and

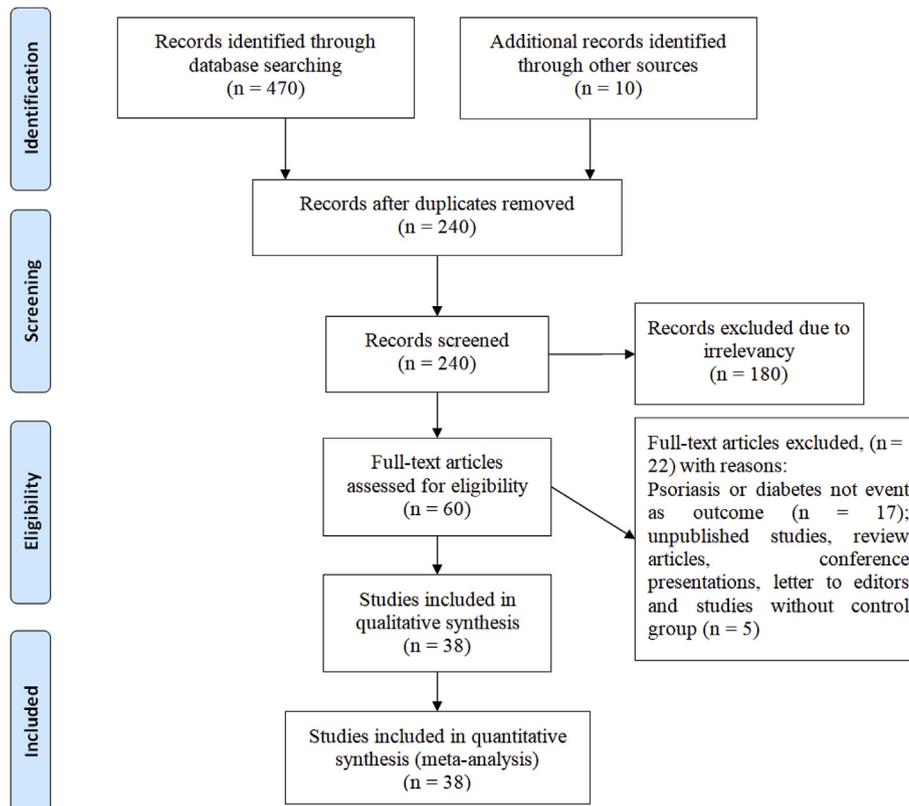


Fig. 1. PRISMA flow diagram.

Begg's tests. Data were presented through flowcharts, summary tables, and funnel plots. The significance level was considered as 0.05.

3. Results

3.1. Study characteristics and methodological quality

After searching the related databases, 480 articles were collected, and 240 duplicate studies were excluded. Then, the abstract of 240 articles was reviewed and 180 irrelevant articles were excluded. The full text of 60 articles were reviewed and 22 articles were excluded (Fig. 1). Finally, 38 studies including 922870 cases with psoriasis and 12808071 controls entered the meta-analysis (Table 1). The mean age in case group was 50.93 (Standard Error [SE]:1.4, $P < 0.001$) and 49.74 (SE: 1.75, $P < 0.001$) in control group.

3.2. Association between psoriasis and diabetes mellitus

Heterogeneity was high in this meta-analysis ($I^2 = 98.5\%$; $P < 0.001$). Meta-analysis of studies showed a combined OR of 1.69 (95% CI: 1.51–1.89; $P < 0.001$) (Fig. 2).

3.3. Sensitivity analysis

Sensitivity analysis showed that point estimate with removal of one study at a time is robust (Fig. 3).

3.4. Subgroup analysis

In subgroup analysis based on the type of study, the OR was estimated 1.86 (95%CI: 1.47–2.35; $P < 0.001$), 1.40 (95%CI: 1.24–1.6; $P < 0.001$) and 1.84 (95%CI: 1.52–2.24; $P < 0.001$) in case-control, cohort and cross-sectional studies, respectively. The test for differences in subgroup analysis was not significant ($p = 0.025$) (Fig. 4).

Subgroup analysis based on country of study was shown in Fig. 5. Test result for differences in subgroup analysis was significant ($p < 0.001$).

3.5. Publication bias

In the Egger and Begg's tests, p -value was estimated to be 0.205 and 0.087 respectively (Fig. 6).

4. Discussion

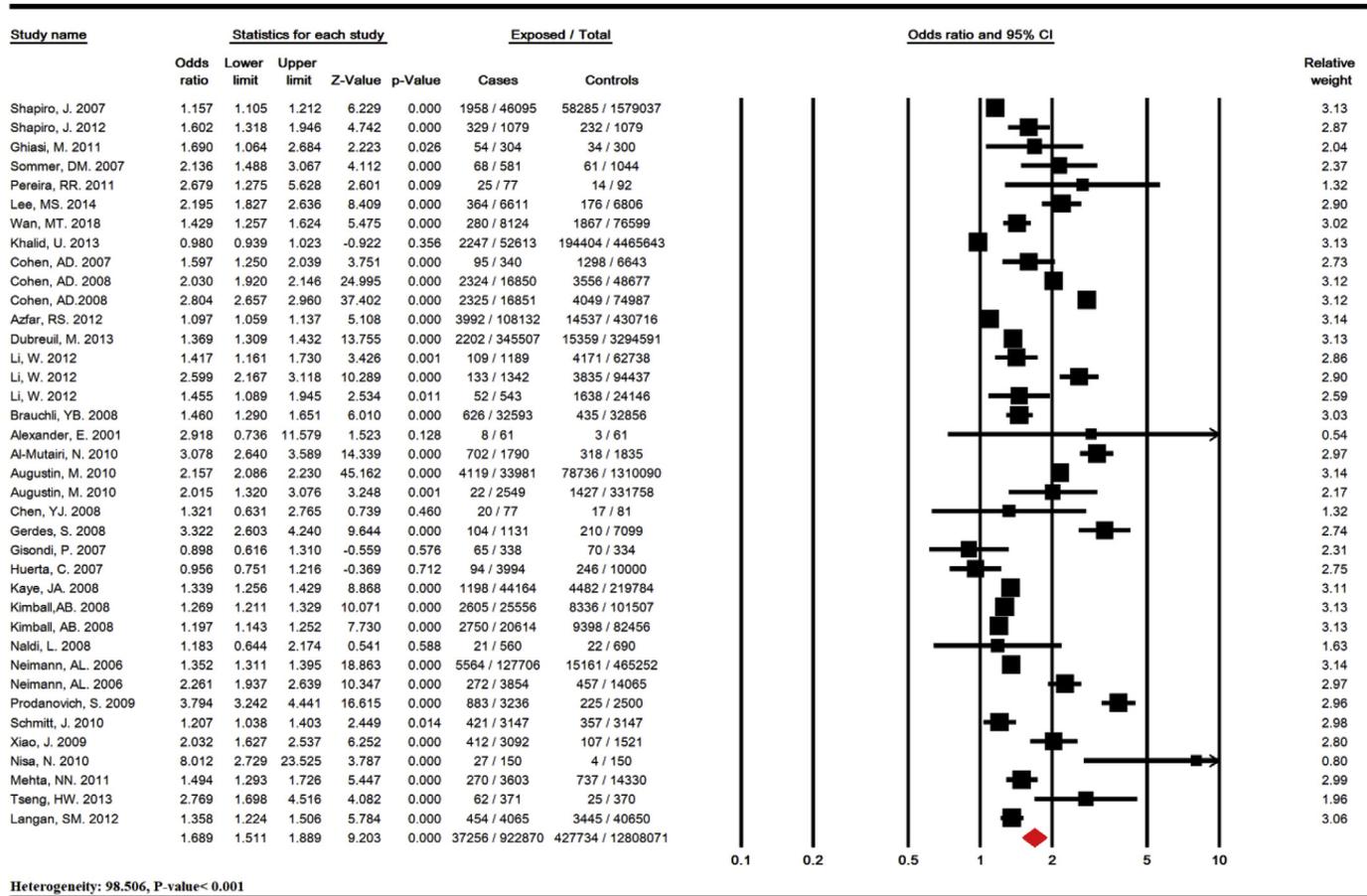
Several studies have been performed on the association be-

Table 1

Data obtained from studies on association between psoriasis and diabetes mellitus.

Author	Year	case	Mean age(SD) ^a	Diabetes positive in case group	control	Mean age(SD)	Diabetes positive in control group
Shapiro [24]	2007	46095	41.28(18.8)	1958	1579037		58285
Shapiro [25]	2012	1079	68.60(15.1)	329	1079	68.7(15.1)	232
Ghiasi [26]	2011	304	41.06(0.44)	54	300	39.74(0.7)	34
Sommer [27]	2007	581	54.4	68	1044	58.5	61
Pereira [28]	2011	77	46.51(13.53)	25	92	43.24(12.33)	14
Lee [29]	2014	6611	42.39(19.45)	364	6806	33.04(20.68)	176
Wan [30]	2018	8124	44.86	280	76599	44.54	1867
Khalid [31]	2013	52613		2247	4465643	43.9(19.9)	194404
Cohen [32]	2007	340	47.7(10.7)	95	6643	47(11)	1298
Cohen [33]	2008	16850	42.7(20.3)	2324	48677	51(19.1)	3556
Cohen [34]	2008	16851	51(19.1)	2325	74987	33.8(23.5)	4049
Azfar [35]	2012	108132	46.03(16.62)	3992	430716	48.4(16.64)	14537
Dubreuil [36]	2013	345507		2202	3294591		15359
Li [37]	2012	1189	61.2(6.8)	109	62738	60.9(6.8)	4171
Li [37]	2012	1342	36.7(4.6)	133	94437	36.2(4.6)	3835
Li [37]	2012	543	50.8(8.1)	52	24146	50.5(8)	1638
Brauchli [38]	2008	32593		626	32856		435
Alexander [39]	2001	61		8	61		3
Al-Mutairi [40]	2010	1790		702	1835	52.7(13.5)	318
Augustin [41]	2010	33981		4119	1310090		78736
Augustin [42]	2010	2549		22	331758		1427
Chen [43]	2008	77	57.39(19.15)	20	81	55.63(5.41)	17
Gerdes [44]	2008	1131		104	7099		210
Gisondi [45]	2007	338	62.1(15.1)	65	334	63.8(20.4)	70
Huerta [46]	2007	3994		94	10000		246
Kaye [47]	2008	44164		1198	219784		4482
Kimball [48]	2008	25556	47.1(12.6)	2605	101507	47.1(12.7)	8336
Kimball [48]	2008	20614	54.9(15.5)	2750	82456	54.9(15.5)	9398
Naldi [49]	2008	560		21	690		22
Neimann [50]	2006	127706	46.4	5564	465252	45.7	15161
Neimann [50]	2006	3854	49.8	272	14065	46.34	457
Prodanovich [51]	2009	3236	67.9(14.1)	883	2500	65.1(17.6)	225
Schmitt [52]	2010	3147	57.1	421	3147	57.1	357
Xiao [53]	2009	3092	43.6	412	1521	43.6	107
Nisa [54]	2010	150		27	150		4
Mehta [55]	2011	3603	52.2(16.7)	270	14330	49.7(19.3)	737
Tseng [56]	2013	371		62	370		25
Langan [57]	2012	4065		454	40650		3445

^a SD: Standard deviation.



Meta Analysis

Fig. 2. Meta-Analysis of Studies on Association of Psoriasis and Diabetes Mellitus (mean point of each segment shows the estimated OR, and the length of each segment shows 95% CI in each study; the diamond mark shows the OR in each study).

tween psoriasis and systemic disease [15,16], and finding a definitive association between these diseases may play an important role in the management of psoriatic patients.

By combining the results of 38 studies, the present study confirmed that patients with psoriasis are at higher the risk of diabetes mellitus, which is consistent with the results of previous meta-analyses. Total OR for the association between psoriasis and diabetes mellitus was 1.69 (95% CI: 1.51–1.89; $P < 0.001$). Heterogeneity in our meta-analysis was high, and therefore, subgroup analysis was conducted, which was significant for the country of study.

The results of our study supported the results of the meta-analysis by Cheng et al. By analyzing 22 studies, they suggested that psoriatic patients are at higher risk of diabetes and OR for this association was 1.42 (95% CI: 1.40–1.45) [17].

Another meta-analysis conducted by Miller et al. suggested that psoriasis increase the risk of diabetes and the OR for this association was 1.9 (95% CI: 1.5–2.5) [18]. In another meta-analysis, the OR for the association between type 2 diabetes mellitus and psoriasis was 1.76 (95% CI: 1.59–1.96) [19].

In a meta-analysis conducted by Samarasekera et al., the risk of cardiovascular disease(CVD) increased in patients with severe psoriasis and the OR was 1.37 (95% CI: 1.17–1.6) for CVD mortality, 3.04 (95% CI: 0.65–14.35) for myocardial infarction (MI), and, 1.59

(95% CI: 1.34–1.89) for stroke [20].

In another study conducted by Singh et al., in 2017, the OR for the association between psoriasis and metabolic syndrome was 2.14 (95% CI: 1.84–2.48) [21].

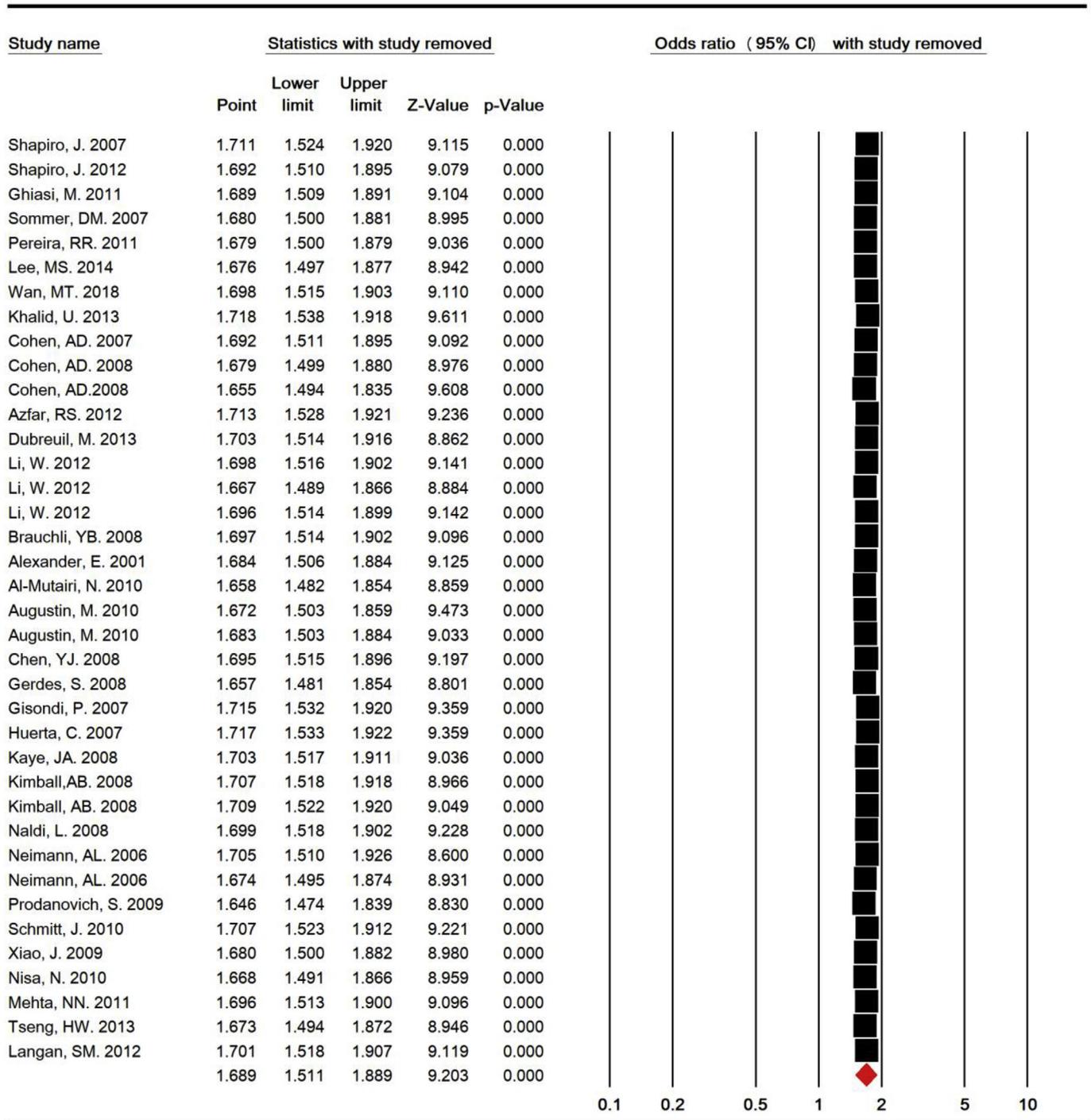
According to related studies, the appearance of psoriasis is on the skin, but psoriasis is a disease that involves more than skin and must be considered as a systemic disorder. In addition, new studies suggest the role of inflammation in pathogenesis of chronic disorders and psoriasis is a chronic inflammatory skin disease [22,23], so underlying inflammation may be the cause of the association between these diseases.

The strength of our study was the large number of studies included in the meta-analysis and subgroup analysis based on country and type of studies. Limitation of our study was lack of mentioning the type of diabetes in some articles. Another limitation was the articles published in other languages, which may lead to bias.

5. Conclusion

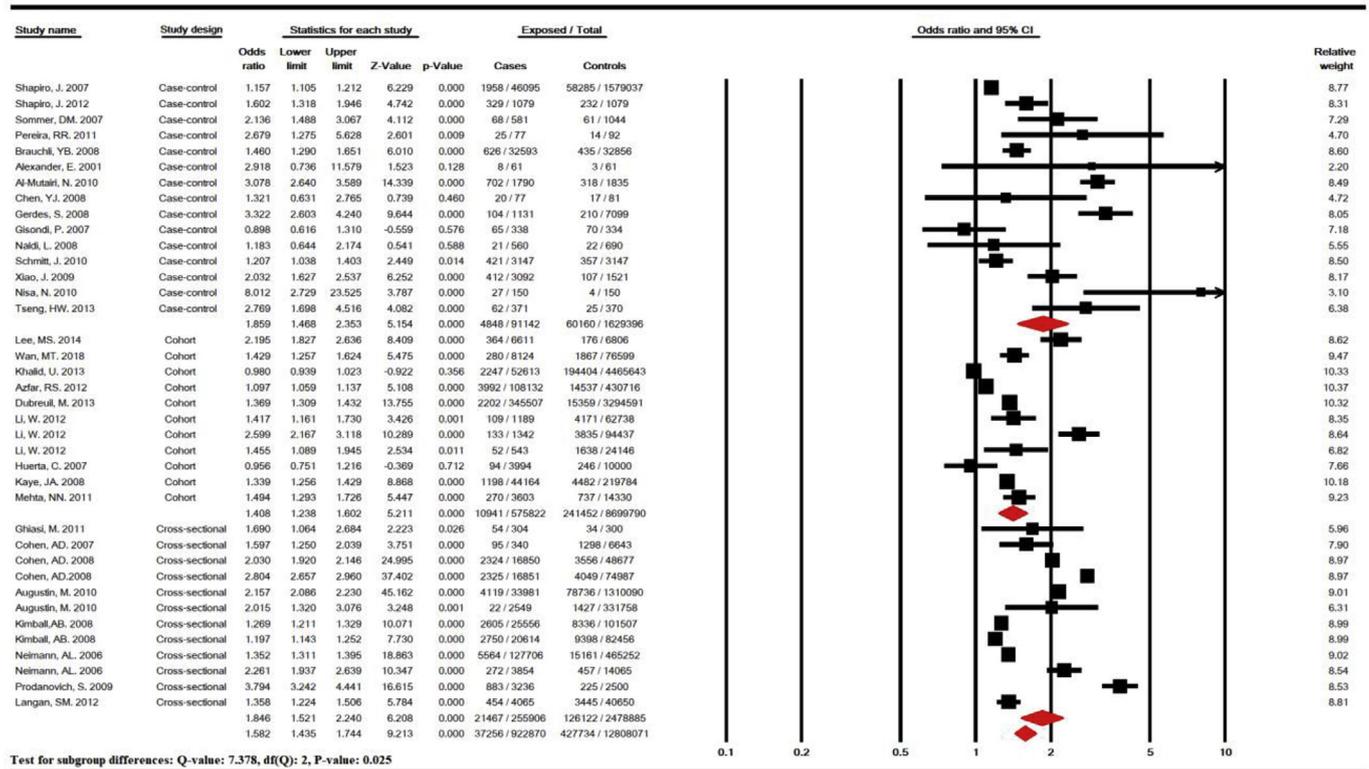
According to the present meta-analysis psoriasis is a systemic disorder so other comorbidities should be considered in management of patients with psoriasis.

There may be a common pathophysiological mechanism for



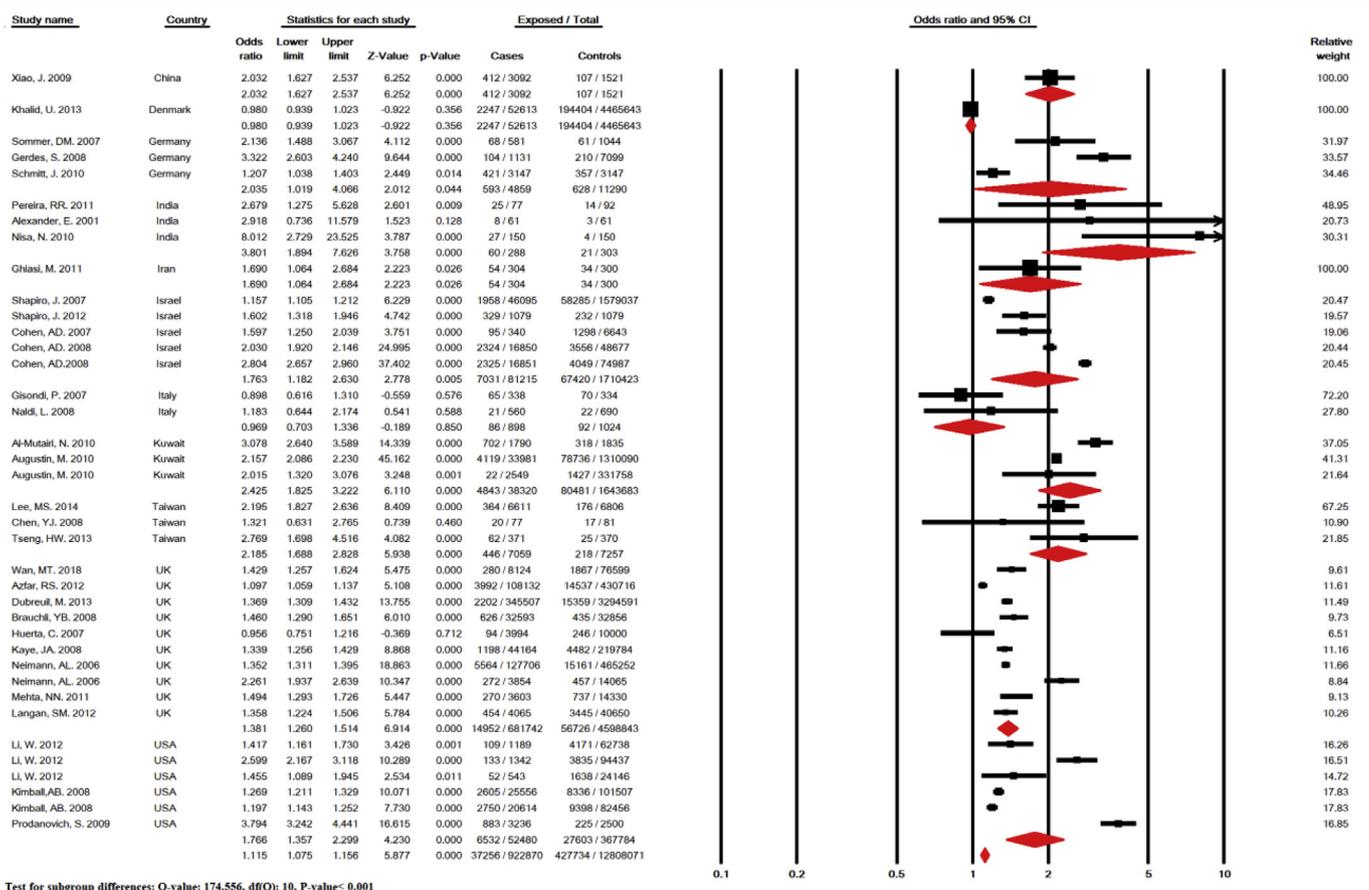
Meta Analysis

Fig. 3. Sensitivity analysis in Meta-Analysis on Association between Psoriasis and Diabetes Mellitus.



Meta Analysis

Fig. 4. Meta-analysis of studies on the association between Psoriasis and Diabetes Mellitus according to type of studies.



Meta Analysis

Fig. 5. Meta-analysis of studies on the association between Psoriasis and Diabetes Mellitus according to country of studies.

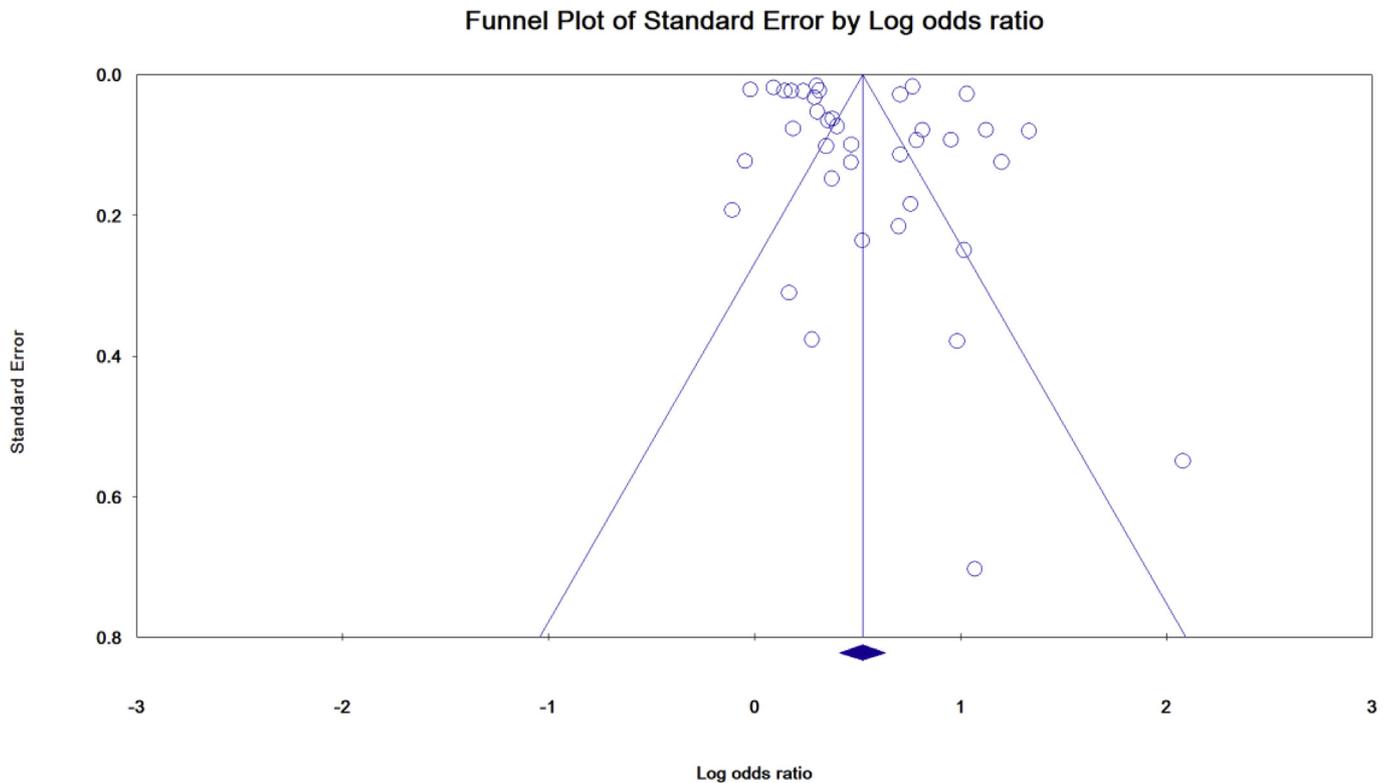


Fig. 6. Publication bias in meta-analysis between studies on association of psoriasis and diabetes mellitus.

psoriasis and diabetes.

Further research is required to better understand the exact association between these two systemic disorders and to find the common pathophysiology mechanism.

Conflicts of interest

None declared.

Financial support

This research was financially supported by Ilam University of Medical Sciences, Iran.

Acknowledgments

Hereby, we extend our gratitude to the Deputy of Research and Education at Ilam University of Medical Sciences for supporting this research project.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.dsx.2019.01.009>.

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